## BREAKING ADVANCES

**Highlights from Recent Cancer Literature**

### REVIEWS

6379  
Decoding the Histone Code: Role of H3K36me3 in Mismatch Repair and Implications for Cancer Susceptibility and Therapy  
Guo-Min Li

6384  
Real-time Liquid Biopsy in Cancer Patients: Fact or Fiction?  
Klaus Pantel and Catherine Aix-Panabieres

## MEETING REPORT

6389  
The Hippo Tumor Suppressor Network: From Organ Size Control to Stem Cells and Cancer  
Georg Halder and Fernando D. Camargo

## PRIORITY REPORT

6393  
Erythropoietin Activates Cell Survival Pathways in Breast Cancer Stem–like Cells to Protect Them from Chemotherapy  
Matilde Todaro, Alice Turdo, Monica Bartucci, Flora Jovino, Rosanna Dattilo, Marco Biffoni, Giorgio Stassi, Giulia Federici, Ruggero De Maria, and Ann Zeuner  
**Précis:** A growth factor that has been used in the oncology clinic to support red blood cell counts in patients receiving chemotherapy is found to counter the therapeutic killing of cancer stem-like cells, offering a mechanistic explanation for why cancer patients receiving this growth factor have shown reduced survival.

## INTEGRATED SYSTEMS AND TECHNOLOGIES

6401  
A Transcriptional and Metabolic Signature of Primary Aneuploidy Is Present in Chromosomally Unstable Cancer Cells and Informs Clinical Prognosis  
Jason M. Sheltzer  
**Précis:** Chromosomal instability in cancer cells is associated with a transcriptional stress response that has prognostic significance in various types of human malignancy.

## MICROENVIRONMENT AND IMMUNOLOGY

6413  
GM-CSF Promotes the Immunosuppressive Activity of Glioma-Infiltrating Myeloid Cells through Interleukin-4 Receptor-α  
Gary Kohanbash, Kayla McKaveney, Masashi Sakaki, Ryo Ueda, Arlan H. Mintz, Nduka Amankulu, Mitsugu Fujita, John R. Ohiest, and Hideho Okada  
**Précis:** These findings reveal the operation of immunosuppressive mechanisms in the glioblastoma microenvironment driven by GM-CSF, a factor used in the clinic to elevate white blood cell counts in patients, suggesting clinical risks arising from its use.

6424  
Substance P Autocrine Signaling Contributes to Persistent HER2 Activation That Drives Malignant Progression and Drug Resistance in Breast Cancer  
Susana Garcia-Recio, Gemma Fuster, Patricia Fernandez-Nogueira, Eva M. Pastor-Arroyo, So Yeon Park, Cristina Mayordomo, Elisabet Ametller, Mario Mancino, Xavier Gonzalez-Farre, Hege G. Russnes, Pablo Engel, Domiziana Costamagna, Pedro L. Fernandez, Pedro Gascon, and Vanessa Almendro  
**Précis:** This work illuminates the oncogenic cooperation between HER2 and a substance P receptor involved in pain signaling, providing a novel link between cancer inflammation and progression that might be targeted by substance P antagonists being explored in the clinic.

## MOLECULAR AND CELLULAR PATHOBIOLOGY

6435  
mir-153 Supports Colorectal Cancer Progression via Pleiotropic Effects That Enhance Invasion and Chemotherapeutic Resistance  
Lei Zhang, Karen Pickard, Veronika Jenei, Marc D. Bullock, Amanda Bruce, Richard Mitter, Gavin Kelly, Cristos Paraskeva, John Streiford, John Primrose, Gareth J. Thomas, Graham Packham, and Alex H. Mirnezami  
**Précis:** MicroRNAs that facilitate progression and mediate drug resistance in advanced cancers have increased appeal as treatment targets, given the more frequent lack of effective therapies at late stages of disease.
Mutationally Activated PIK3CA<sup>H1047R</sup>
Cooperates with BRAF<sup>V600E</sup> to Promote Lung Cancer Progression
Christy L. Trejo, Shon Green, Victoria Marsh, Eric A. Collisson, Gioia Iezza, Wayne A. Phillips, and Martin McMahon

**Précis:** These findings deepen the in vivo evidence that MAPK and PI3K signaling cooperates in mediating the development and progression of KRAS-mutated lung cancer, suggesting combination therapies to treat this disease.

Antitumor Efficacy of a Monoclonal Antibody That Inhibits the Activity of Cancer-Associated Carbonic Anhydrase XII
Gabor Gondi, Josef Mysliwietz, Alzbeta Hulikova, Jian Ping Jen, Pawel Swietach, Elisabeth Kremmer, and Reinhard Zeidler

**Précis:** This study offers a preclinical proof-of-concept for immune targeting a cell surface carbonic anhydrase that is widely expressed in human cancer as a general therapeutic strategy.

**THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY**

Photodynamic Therapy of Murine Mastocytoma Induces Specific Immune Responses against the Cancer/Testis Antigen P1A
Pawel Mroz, Fatma Vatansever, Angelika Muchowicz, and Michael R. Hamblin

**Précis:** Effective photodynamic therapy used to treat certain cancers may act as antigen-specific immunotherapy.

Bispecific Antibody to ErbB2 Overcomes Trastuzumab Resistance through Comprehensive Blockade of ErbB2 Heterodimerization
Bohua Li, Yanchun Meng, Lei Zheng, Xunmin Zhang, Qing Tong, Wenlong Tan, Shi Hu, Hui Li, Yang Chen, Jinqing Song, Ge Zhang, Lei Zhao, Dapeng Zheng, Sheng Hou, Weizhu Qian, and Yajun Guo

**Précis:** Using a bispecific antibody to block ErbB2/HER2 heterodimerization on the surface of breast cancer cells may provide a strategy to overcome resistance to Herceptin that remains a major clinical challenge in breast cancer patients.

A Small-Molecule Blocking Ribonucleotide Reductase Holoenzyme Formation Inhibits Cancer Cell Growth and Overcomes Drug Resistance

**Précis:** These findings address deficiencies in existing drugs that block ribonucleotide reductase, offering preclinical validation of a promising new class of inhibitors against this valid target that could find broad use to treat many human cancers.

MYC Phosphorylation at Novel Regulatory Regions Suppresses Transforming Activity
Amanda R. Wasylishen, Michelle Chan-Seng-Yue, Christina Rros, Dharmendra Dingar, William B. Tu, Manpreet Kalkat, Pak-Kei Chan, Peter J. Mullen, Ling Huang, Natalie Meyer, Brian Raught, Paul C. Boutros, and Linda Z. Penn

**Précis:** MYC phosphorylation mutants with super-transforming activity that were identified in this study point the way toward new therapeutic targets to attack MYC by a backdoor approach.

**TUMOR AND STEM CELL BIOLOGY**

Nitric Oxide Production Upregulates Wnt/β-Catenin Signaling by Inhibiting Dickkopf-1
Qiang Du, Xinglu Zhang, Quan Liu, Xianghong Zhang, Christian E. Bartels, and David A. Geller

**Précis:** In addressing the complex role of nitric oxide in cancer, this study furthers evidence of an oncogenic contribution that is mediated by a mechanism that stimulates Wnt/β-catenin signaling, a central pathway for carcinogenesis.

**CORRECTION**

Correction: Breast Tumor Kinase (Brk/PTK6) Is a Mediator of Hypoxia-Associated Breast Cancer Progression
miR-153 leads to increased invasiveness in colorectal cancer. Using mouse tumor xenografts, it was found that colorectal tumors with inhibition of miR-153 show a clean edge of tumor spheroid and fewer invasive fronts into the surrounding stroma (magnification, ×400) in contrast to controls with a more locally invasive tumor phenotype. For details, see article by Zhang and colleagues on page 6435.